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 NEWS WWW       CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:53:06 ON 12 NOV 2002

=> file registry
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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 14:53:17 ON 12 NOV 2002
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STRUCTURE FILE UPDATES:   11 NOV 2002  HIGHEST RN 473219-67-9
DICTIONARY FILE UPDATES:  11 NOV 2002  HIGHEST RN 473219-67-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09734460a.str

L1      STRUCTURE UPLOADED

=> d L1
L1 HAS NO ANSWERS
L1              STR
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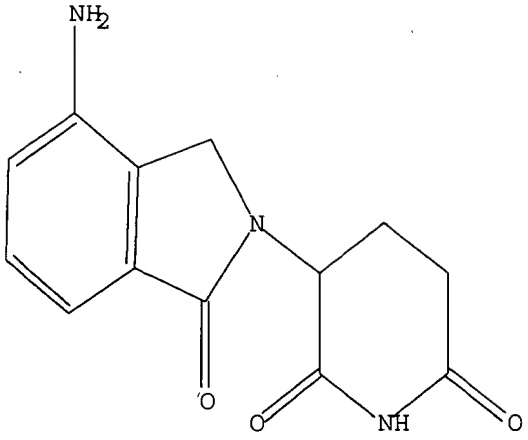

Structure attributes must be viewed using STN Express query preparation.

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=> s L1 sam exa
SAMPLE SEARCH INITIATED 14:53:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      1 TO ITERATE

100.0% PROCESSED       1 ITERATIONS                          0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA EXA SAM L1

=> s L1 exa full
FULL SEARCH INITIATED 14:54:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     16 TO ITERATE

100.0% PROCESSED      16 ITERATIONS                          2 ANSWERS
SEARCH TIME: 00.00.02

L3             2 SEA EXA FUL L1

=> d L3 1-2

L3   ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2002 ACS
RN   202271-91-8  REGISTRY
CN   2,6-Piperidinedione, 3-(4-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-, (S)-
     (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C13 H13 N3 O3
SR   CA
LC   STN Files:   CA, CAPLUS

Absolute stereochemistry.
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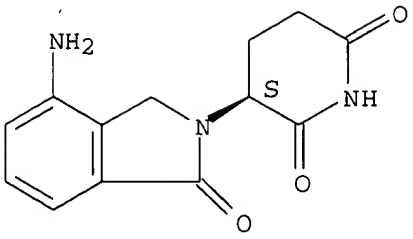
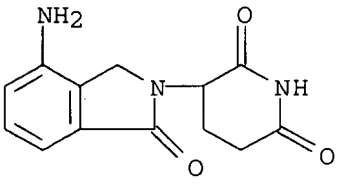


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L3 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2002 ACS
RN 191732-72-6 REGISTRY
CN 2,6-Piperidinedione, 3-(4-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3-(4-Amino-1-oxoisoindolin-2-yl)piperidine-2,6-dione
FS 3D CONCORD
MF C13 H13 N3 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1962 TO DATE)
5 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	50.92	51.13

FILE 'CAPLUS' ENTERED AT 14:54:40 ON 12 NOV 2002
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FILE COVERS 1907 - 12 Nov 2002 VOL 137 ISS 20
FILE LAST UPDATED: 11 Nov 2002 (20021111/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s L3
L4 6 L3

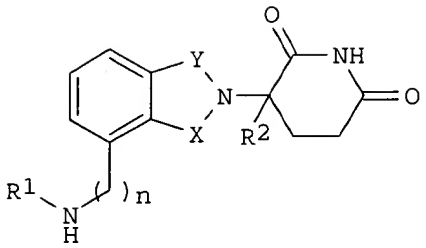
=> d L4 1-6 ibib,abs,kwic

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:575064 CAPLUS
DOCUMENT NUMBER: 137:125091
TITLE: Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as TNF-.alpha. inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders
INVENTOR(S): Robarge, Michael J.; Chen, Roger Shen-Chu; Muller, George W.; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 224 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

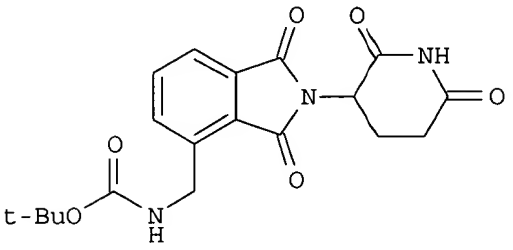
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059106	A1	20020801	WO 2001-US50401	20011221

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-258372P P 20001227
US 2001-972487 A 20011005
OTHER SOURCE(S): MARPAT 137:125091
GI



I



II

AB Title isoindole-imides I [wherein one of X and Y is CO and the other is CH2 or CO; R1 = H, (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, COR3, CSR3, CO2R4, alkyl-(NR6)2, alkyl-OR5, alkyl-CO2R5, CONHR3, CSNHR3, CON(R3)2, CSN(R3)2, or alkyl-OCOR5; R2 = H, benzyl, alkyl, alkenyl, or alkynyl; R3 = independently (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, alkyl-N(R6)2, alkyl-OR5, alkyl-CO2R5, alkyl-OCOR5, or CO2R5; R4 = alkyl, alkenyl, alkynyl, alkyl-OR5, benzyl, aryl, alkylheterocycloalkyl, or alkylheteroaryl; R5 = alkyl, alkenyl, alkynyl, benzyl, aryl, or heteroaryl; R6 = independently H, alkyl, alkenyl, alkynyl, benzyl, (hetero)aryl, or alkyl-CO2R5; or R6 groups may join to form a heterocycloalkyl group; n = 0-1; with the proviso that when n = 0, R1 .noteq. H; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, enantiomers, diastereomers, racemates, or mixts. of stereoisomers thereof] were prepd. for reducing the level of cytokines and their precursors in mammals. In particular, the invention pertains to isoindole-imide compds. that are potent inhibitors of the prodn. of TNF-.alpha. (no data). For example, Me 2-(methoxycarbonyl)-3-nitrobenzoate was hydrogenated with 10% Pd/C (87%). The amine was converted to the nitrile by diazonium salt formation effected by treatment with NaNO3 followed by cyanide formation using classic Sandmeyer procedure (65%). The nitrile was reduced with 10% Pd/C in MeOH and aq. HCl under hydrogen to afford Me 3-aminomethyl-2-(methoxycarbonyl)benzoate.bul.HCl (90%), which was treated with TEA and then reacted with di-t-Bu dicarbonate to give the carbamate (93%). Cyclization with 3-aminoglutarimide.bul.HCl using diisopropylethylamine in DMF produced II (82%). The 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones and pharmaceutical compns. comprising them are useful for treating or preventing diseases or disorders in mammals, e.g. cancers, such as solid tumors and blood-born tumors; heart disease, such as congestive heart failure; osteoporosis; and genetic, inflammatory, allergic, and autoimmune diseases (no data).

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 67-47-0, 5-Hydroxymethylfuran-2-carboxaldehyde 79-03-8, Propionyl chloride 79-04-9, Chloroacetyl chloride 79-30-1, Isobutyryl chloride 98-01-1, Furan-2-carboxaldehyde, reactions 98-03-3, 2-Thiophenecarboxaldehyde 98-88-4, Benzoyl chloride 100-52-7, Benzaldehyde, reactions 103-71-9, Phenyl isocyanate, reactions 103-80-0, 2-Phenylacetyl chloride 109-89-7, Diethylamine, reactions 109-90-0, Ethyl isocyanate 110-62-3, Valeraldehyde 110-78-1, Propyl

isocyanate 111-36-4, n-Butyl isocyanate 111-71-7, Heptanal 121-90-4, 3-Nitrobenzoyl chloride 122-01-0, 4-Chlorobenzoyl chloride 122-04-3, 4-Nitrobenzoyl chloride 141-75-3, Butanoyl chloride 329-15-7, 4-(Trifluoromethyl)benzoyl chloride 393-52-2, 2-Fluorobenzoyl chloride 403-43-0, 4-Fluorobenzoyl chloride 500-22-1, 3-Pyridinecarboxaldehyde 501-53-1, Benzyl chloroformate 527-69-5, 2-Furoyl chloride 542-85-8, Ethyl isothiocyanate 587-04-2, 3-Chlorobenzaldehyde 618-46-2, 3-Chlorobenzoyl chloride 627-03-2, Ethoxyacetic acid 638-29-9, Pentanoyl chloride 701-99-5, Phenoxyacetyl chloride 874-60-2, 4-Methylbenzoyl chloride 1490-25-1, Methyl 3-(chlorocarbonyl)propanoate 1609-86-5, tert-Butyl isocyanate 1711-05-3, m-Anisoyl chloride 1711-06-4, m-Toluoyl chloride 1711-07-5, 3-Fluorobenzoyl chloride 1795-48-8, Isopropyl isocyanate 1947-00-8, 6-Benzyloxycarbonylaminohexanoic acid 2251-65-2, 3-Trifluoromethylbenzoyl chloride 2444-37-3, (Methylthio)acetic acid 2528-61-2, Heptanoyl chloride 2719-27-9, Cyclohexanecarbonyl chloride 2999-46-4, Ethyl isocyanoacetate 3158-26-7, Octyl isocyanate 3173-53-3, Cyclohexyl isocyanate 3173-56-6, Benzyl isocyanate 3303-84-2 4023-34-1, Cyclopropylcarbonyl chloride 4265-16-1, Benzofuran-2-carboxaldehyde 4524-93-0, Cyclopentanecarbonyl chloride 5271-67-0, 2-Thiophenecarbonyl chloride 5781-53-3, Methyl (chlorocarbonyl)formate 7065-46-5, tert-Butylacetyl chloride 10400-19-8, Nicotinoyl chloride 13365-26-9, Methyl 2-(methoxycarbonyl)-3-nitrobenzoate 13529-17-4, 5-Formylfuran-2-carboxylic acid 13831-31-7, Acetoxyacetyl chloride 14794-32-2, 6-(Chloroformyl)hexanoic acid ethyl ester 17746-05-3, Undecanoyl chloride 19171-19-8, 4-Amino-2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-dione 19810-31-2, Benzyloxyacetyl chloride 20260-53-1, Nicotinoyl chloride hydrochloride 21615-34-9, 2-Methoxybenzoyl chloride 24424-99-5, BOC-anhydride 24666-56-6, Glutamimide hydrochloride 38870-89-2, Methoxyacetyl chloride 39741-62-3 39901-94-5, Pyridine-2-carbonyl chloride hydrochloride 41904-40-9 52480-43-0, 4,5-Dimethylfuran-2-carboxaldehyde 57260-71-6 60142-89-4, N-BOC-7-aminoheptanoic acid 60656-87-3, Benzyloxyacetaldehyde 73839-06-2, 3-Amino-3-methylpiperidine-2,6-dione monohydrochloride 76006-33-2, 3-Bromo-2-methylbenzoic acid 124949-23-1, 4-Nitrophenyl N-cyclopentylcarbamate **191732-72-6**, 3-(4-Amino-1-oxoisoindolin-2-yl)piperidine-2,6-dione 202271-87-2, 4-Amino-2-(3-methyl-2,6-dioxopiperidin-3-yl)isoindole-1,3-dione 444287-94-9, 3-(2-Methoxyethylamino)phthalic acid 444287-98-3, 3-Pentylaminophthalic acid 444288-03-3, 3-(2-Benzyloxyethylamino)phthalic acid 444288-42-0 444288-59-9, 3-[(5-Methylfuran-2-ylmethyl)amino]phthalic acid 444288-63-5, 3-[(5-Hydroxymethylfuran-2-ylmethyl)amino]phthalic acid 444288-68-0, 3-[(Thiophen-2-ylmethyl)amino]phthalic acid 444288-74-8, 3-(3-Chlorobenzylamino)phthalic acid 444288-77-1, 3-[(Pyridin-3-ylmethyl)amino]phthalic acid 444288-80-6, 3-[(5-Carboxyfuran-2-ylmethyl)amino]phthalic acid 444288-83-9, 3-[(4,5-Dimethylfuran-2-ylmethyl)amino]phthalic acid 444288-87-3, 3-[(Benzofuran-2-ylmethyl)amino]phthalic acid 444288-94-2 444289-00-3, 4-(Aminomethyl)-2-(3-methyl-2,6-dioxo-3-piperidyl)isoindoline-1,3-dione monohydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of (oxopiperidyl)isoindolinone TNF-.alpha. inhibitors by cycloaddn. of aminoglutarimides to carboxybenzoates)

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:452859 CAPLUS
DOCUMENT NUMBER: 135:51096
TITLE: Compositions for the prevention and treatment of atherosclerosis and restenosis
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043743	A1	20010621	WO 2000-US33708	20001213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002054899	A1	20020509	US 2000-734460	20001211
EP 1242082	A1	20020925	EP 2000-984269	20001213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 1999-170820P P 19991215
WO 2000-US33708 W 20001213

AB Methods and compns. for the prevention and treatment of all forms of atherosclerosis are described. Administration of compds. such as thalidomide, its analogs, hydrolysis products, metabolites, derivs. and precursors as well as addnl. compds. capable of inhibiting tumor necrosis factor-.alpha. (TNF-.alpha.) are used in the invention. Also disclosed is the coating of prosthetic devices, such as stents, with the compds. of the invention for the prevention and/or treatment of restenosis. Tablets contained 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline 50.0, lactose 50.7, wheat starch 7.5, PEG-6000 5.0, talc 5.0, and Mg stearate 1.8 and water qs.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 50-35-1, Thalidomide 50-35-1D, Thalidomide, analogs 50-35-1D, derivs. 100-42-5D, Styrene, derivs. 19171-19-8 26581-81-7D, derivs. 167886-76-2 **191732-72-6** 220460-55-9D, derivs. 220460-63-9D, derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. for prevention and treatment of atherosclerosis and restenosis)

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:386135 CAPLUS
DOCUMENT NUMBER: 131:129881
TITLE: Amino-substituted thalidomide analogs: potent inhibitors of TNF-.alpha. production
AUTHOR(S): Muller, George W.; Chen, Roger; Huang, Shaei-Yun; Corral, Laura G.; Wong, Lu Min; Patterson, Rebecca T.; Chen, Yuxi; Kaplan, Gilla; Stirling, David I.
CORPORATE SOURCE: Celgene Corporation, Warren, NJ, 07059, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(11), 1625-1630
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thalidomide is a known inhibitor of TNF-.alpha. release in LPS stimulated human PBMC. Herein we describe the TNF-.alpha. inhibitory activity of amino substituted analogs of thalidomide and its isoindolin-1-one analog, EM-12. The 4-amino substituted analogs were found to be potent inhibitors

of TNF-.alpha. release in LPS stimulated human PBMC.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

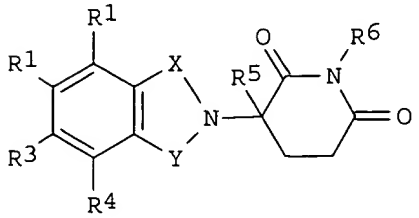
IT 19171-19-8P 191732-70-4P **191732-72-6P** 191732-74-8P
191732-75-9P 191732-76-0P 202271-87-2P 202271-89-4P 202271-90-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(amino derivs. of thalidomide and EM-12 as inhibitors of TNF-.alpha. prodn.)

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:795004 CAPLUS
DOCUMENT NUMBER: 130:38290
TITLE: Substituted 2-(2,6-dioxopiperidin-3-yl)phthalimides and 1-oxoisoindolines and method of reducing tnf.alpha. levels
INVENTOR(S): Muller, George W.; Stirling, David I.; Chen, Roger Shen-chu
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

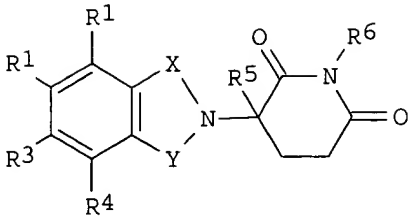
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854170	A1	19981203	WO 1998-US10886	19980528
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877012	A1	19981230	AU 1998-77012	19980528
AU 741982	B2	20011213		
EP 984955	A1	20000315	EP 1998-924959	19980528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002501536	T2	20020115	JP 1999-500909	19980528
FI 9902490	A	20000127	FI 1999-2490	19991123
NO 9905751	A	20000128	NO 1999-5751	19991123
US 6395754	B1	20020528	US 2000-445002	20000222

PRIORITY APPLN. INFO.: US 1997-48278P P 19970530
WO 1998-US10886 W 19980528

OTHER SOURCE(S): MARPAT 130:38290
GI



I



I

AB Substituted 2-(2,6-dioxopiperidin-3-yl)phthalimides and 1-oxo-2-(2,6-dioxopiperidin-3-yl)isoindolines (I) (one of X and Y = CO and the other is CH2 or CO; R1, R2, R3, R4 independently is halo, C1-4-alkyl or -alkoxy or one of R1, R2, R3, R4 is (un)substituted NH2 and the others are H; R5 = H or C1-8-alkyl, benzo, Cl, F; R6 = substituted CH2O(CO)R8CH2NH2 (R8 = m- or p-phenylene of (CH2)n (n = 1-4))) were claimed to reduce the levels of TNF.alpha. in a mammal. I (R6 = H) were prepd. and used in pharmaceutical compns. Thus 1-oxo-2-(2,6-dioxo-3-methylpiperidin-3-yl)-4,5,6,7-tetrafluoroisoindoline was prepd. in a multistep reaction initially from methylglutamic acid which was converted via many steps to .alpha.-amino-.alpha.-methylglutarimide which was converted visa many steps to the final product.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **191732-72-6** 216669-14-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and redn. of TNF.alpha. levels by)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:87727 CAPLUS
DOCUMENT NUMBER: 128:140615
TITLE: Substituted 2-(2,6-dioxo-3-piperidinyl)phthalimides and -1-oxoisoindolines and method of reducing TNF-.alpha. levels
INVENTOR(S): Muller, George W.; Stirling, David I.; Chen, Roger Shen-chu
PATENT ASSIGNEE(S): Celgene Corp., USA; Muller, George W.; Stirling, David I.; Chen, Roger Shen-Chu
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803502	A1	19980129	WO 1997-US13375	19970724
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5635517	A	19970603	US 1996-690258	19960724
US 5635517	B1	19990629		
US 5798368	A	19980825	US 1996-701494	19960822
AU 9738998	A1	19980210	AU 1997-38998	19970724
AU 715779	B2	20000210		
EP 925294	A1	19990630	EP 1997-936295	19970724

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

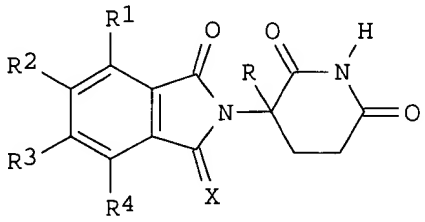
JP 2001503384	T2	20010313	JP 1998-507259		19970724
RU 2177944	C2	20020110	RU 1999-103124		19970724
FI 9900101	A	19990319	FI 1999-101		19990119
US 6281230	B1	20010828	US 2000-543809		20000406
US 6476052	B1	20021105	US 2000-633908		20000807
US 6316471	B1	20011113	US 2000-634061		20001017
US 6335349	B1	20020101	US 2000-716528		20001120
US 2002045643	A1	20020418	US 2001-781179		20010212

PRIORITY APPLN. INFO.:

US 1996-690258	A	19960724
US 1996-701494	A	19960822
WO 1994-US7411	A	19940701
US 1996-701499	A1	19960724
US 1997-48278P	P	19970530
WO 1997-US13375	W	19970724
US 1999-230389	B3	19990507
US 2000-543804	A3	20000406
US 2000-543809	A1	20000406

OTHER SOURCE(S): MARPAT 128:140615

GI



I

AB Title compds. I (X = O, H2; R = H, alkyl, benzyl, halo; R1, R2, R3, R4 = H, alkyl, alkoxy, halo, amino) were prepd. for TNF-.alpha. redn. in mammals. Thus, I (X = O, R = R1 = R3 = R4 = H, R2 = NO2), prepd. from 4-nitrophthalic anhydride and .alpha.-aminoglutarimide hydrochloride, was hydrogenated over 10% Pd/C in 1,4-dioxane at 50 psi for 6.5 h to give 69% I (X = O, R = R1 = R3 = R4 = H, R2 = NH2). Several examples of formulations were given.

IT 191732-76-0P 202271-86-1P 202271-87-2P 202271-88-3P 202271-89-4P 202271-90-7P **202271-91-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2-(2,6-dioxo-3-piperidinyl)phthalimides and -1-oxoisoindolines for reducing TNF-.alpha. levels)

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:375290 CAPLUS
DOCUMENT NUMBER: 127:86110
TITLE: Method of reducing TNF.alpha. levels with amino-substituted 2-(2,6-dioxopiperidin-3-yl)-1-oxo- and 1,3-dioxoisoindolines
INVENTOR(S): Muller, George W.; Stirling, David I.; Chen, Roger S. -c
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

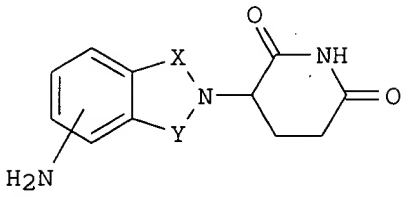
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5635517	A	19970603	US 1996-690258	19960724
US 5635517	B1	19990629		
CA 2261762	AA	19980129	CA 1997-2261762	19970724
WO 9803502	A1	19980129	WO 1997-US13375	19970724
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738998	A1	19980210	AU 1997-38998	19970724
AU 715779	B2	20000210		
EP 925294	A1	19990630	EP 1997-936295	19970724
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1239959	A	19991229	CN 1997-180299	19970724
JP 2001503384	T2	20010313	JP 1998-507259	19970724
RU 2177944	C2	20020110	RU 1999-103124	19970724
FI 9900101	A	19990319	FI 1999-101	19990119
US 6281230	B1	20010828	US 2000-543809	20000406
US 6476052	B1	20021105	US 2000-633908	20000807
US 6316471	B1	20011113	US 2000-634061	20001017
US 6335349	B1	20020101	US 2000-716528	20001120
US 2002045643	A1	20020418	US 2001-781179	20010212

PRIORITY APPLN. INFO.:

WO 1994-US7411	A	19940701
US 1996-690258	A	19960724
US 1996-701499	A1	19960724
US 1996-701494	A	19960822
US 1997-48278P	P	19970530
WO 1997-US13375	W	19970724
US 1999-230389	B3	19990507
US 2000-543804	A3	20000406
US 2000-543809	A1	20000406

OTHER SOURCE(S): MARPAT 127:86110

GI



I

AB 1-Oxo- and 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)isoindolines (I; 1 of X, Y = C:O; other of X, Y = C:O, CH2) substituted with amino in the benzo ring are prepd. which reduce the levels of TNF.alpha. in a mammal. I are therefore useful in treatment of inflammatory, infectious, immunol., or malignant diseases. Thus, 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)-5-aminoisoindoline (II) was prepd. by catalytic hydrogenation of the corresponding 5-nitro compd. (prepd. from 4-nitrophthalic anhydride and .alpha.-aminoglutarimide-HCl) over Pd/C. Tablets each contg. 50 mg II were prepd. from a mixt. of II 50.0, lactose 50.7, wheat starch 7.5, PEG-6000 5.0, talc 5.0, Mg stearate 1.8 g, and sufficient water for granulation.

```
IT   19171-19-8P   191732-70-4P 191732-72-6P   191732-74-8P
     191732-75-9P   191732-76-0P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (method of reducing TNF.alpha. levels with amino-substituted
        dioxopiperidinyloxo- and dioxoisoindolines)


=> file stng
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    16.62      67.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -3.72      -3.72

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Nov  8, 2002 (20021108/UP).

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L2           0 S L1 SAM EXA
L3           2 S L1 EXA FULL

     FILE 'CAPLUS' ENTERED AT 14:54:40 ON 12 NOV 2002
L4           6 S L3

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.48      68.23

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                     0.00      -3.72

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FILE CONTENT: 1988-PRESENT (VOL 104 ISS 15-VOL 137 ISS 19)(20021108/ED)
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MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US    6462221 08 OCT 2002
DE   10118076 17 OCT 2002
EP    1247829 09 OCT 2002
JP 2002302484 18 OCT 2002
WO 2002080929 17 OCT 2002

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higher limits.

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SAMPLE SEARCH INITIATED 15:01:11 FILE 'MARPAT'
SAMPLE SCREEN SEARCH COMPLETED -    170 TO ITERATE

100.0% PROCESSED     170 ITERATIONS                              3 ANSWERS
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         2623 TO     4177
PROJECTED ANSWERS:               3 TO      164

L5             3 SEA SSS SAM L1

=> d L5 1-3 ibib,kwic,abs
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CBIB ----- AN, plus Compressed Bibliographic Data
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IND ------ Indexing Data
IPC ------ International Patent Classifications
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           no answer numbers)
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IABS ----- ABS, indented with text labels
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IBIB ----- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD ----- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels
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SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

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L5 ANSWER 1 OF 3 MARPAT COPYRIGHT 2002 ACS
AN 137:232561 MARPAT
TI Glutarimide derivatives (thalidomide analogs and homologs) with antiangiogenic and TNF-.alpha. inhibitory activity, useful as therapeutic agents in anticancer therapy
IN Fernandez Brana, Miguel; Anorbe Diaz, Loreto; Dominguez Martin, Gema
PA Fundacion Universitaria San Pablo Ceu, Spain
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA Spanish
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002070480	A1	20020912	WO 2002-ES92	20020301
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	ES 2172474	A1	20020916	ES 2001-488	20010301
PRAI	ES 2001-488		20010301		

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 MARPAT COPYRIGHT 2002 ACS
AN 131:214197 MARPAT
TI Preparation of 2-(2,6-dioxo-3-fluoropiperidin-3-yl)isoindolines for reducing inflammatory cytokine levels.
IN Muller, George W.; Stirling, David I.; Chen, Roger Shen-chu; Man, Hon-wah
PA Celgene Corp., USA
SO U.S., 12 pp., Cont. -in-part of U. S. 5,874,448.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5955476	A	19990921	US 1998-42274	19980313
	US 5874448	A	19990223	US 1997-976140	19971118

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     CA 2317834         AA   19990916       CA 1998-2317834  19981117
     WO 9946258         A1   19990916       WO 1998-US24453  19981117
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9914138         A1   19990927       AU 1999-14138    19981117
     EP 1062214         A1   20001227       EP 1998-958016   19981117
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002506068      T2   20020226       JP 2000-535637   19981117
     BR 9815613         A    20020528       BR 1998-15613    19981117
     NO 2000002529      A    20000630       NO 2000-2529     20000516
     FI 2000001192      A    20000714       FI 2000-1192     20000518
PRAI US 1997-976140   19971118
     US 1998-42274    19980313
     WO 1998-US24453  19981117
RE.CNT  29    THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5   ANSWER 3 OF 3  MARPAT  COPYRIGHT 2002 ACS
AN   130:168244  MARPAT
TI   Substituted 2-(2,6-dioxo-3-fluoropiperidin-3-yl)isoindolines and method of
     reducing TNF.alpha. levels
IN   Muller, George W.; Stirling, David I.; Chen, Roger Shen-Chu; Man, Hon-Wah
PA   Celgene Corporation, USA
SO   U.S., 10 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
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PI   US 5874448          A    19990223       US 1997-976140   19971118
     US 5955476          A    19990921       US 1998-42274    19980313
     NO 2000002529       A    20000630       NO 2000-2529     20000516
     FI 2000001192       A    20000714       FI 2000-1192     20000518
PRAI US 1997-976140   19971118
     US 1998-42274    19980313
     WO 1998-US24453  19981117
RE.CNT  3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 27	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
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NEWS 29	Oct 24	BEILSTEIN adds new search fields
NEWS 30	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 31	Oct 25	MEDLINE SDI run of October 8, 2002

NEWS EXPRESS	October 14 CURRENT WINDOWS VERSION IS V6.01, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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